REMARKS

Claims 1-24 are pending in this application. Claims 12-24 have been withdrawn from consideration as being drawn to non-elected invention. Claims 1-11 were rejected under 35 U.S.C. § 103(a).

By this amendment, claim 1 has been amended and claim 25 has been added without prejudice or disclaimer of any previously claimed subject matter. Support for the new claim and amendments can be found, *inter alia*, throughout the specification, for example, at page 6, lines 8-9, at page 13, lines 3-6, and at page 26, lines 19-23. The claims have herein been amended to more clearly reflect Applicants' discovery that cpn10 and IFN-β act co-operatively to relieve symptoms of MS. This co-operative activity allows for administration of cpn10 or IFN-β in amounts that are suboptimal when the agents are administered alone. As demonstrated in the specification, this cooperative activity is particularly effective in delaying relapse of MS. Accordingly, Applicants respectfully request entry and consideration of the claim amendment.

With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Applicants have carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Rejection under 35 U.S.C. §103(a)

Claims 1-11 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Morton *et al.* (WO 95/15338; "Morton") in view of The Interferon Beta Multiple Sclerosis Study Group (Neurology, 1993, 43:655-661; "the MS Study"). Applicants respectfully traverse this rejection.

As amended herein, the invention of claims 1-24 is directed to a method of treating MS through administering a combination of cpn10 and IFN-β in pharmaceutically effective amounts, where the amounts of cpn10 and IFN-β are suboptimal when administered alone. As discussed in the specification, the combination of cpn10 and IFN-β provides greater relief from disease symptoms than either agent alone and thereby reduces the need for IFN-β to be administered at doses which produce side-effects.[1]

Morton describes the use of chaperonin 10 (cpn10) for the treatment of experimental allergic encephalomyelitis (EAE), a standard animal model for multiple sclerosis (MS). Morton does not describe administration of IFN-β. The MS Study describes use of IFN-β for the treatment of MS but is silent with regard to cpn10. Neither reference teaches or suggests the combination of cpn10 and IFN-β for the treatment of MS. Neither Morton nor the MS Study, nor the combination thereof, teaches or suggests that cpn10 and IFN-β act in a co-operative manner or that a combination of cpn10 and IFN-β will result in a therapeutic response when the cpn10 and IFN-β are administered in amounts that are suboptimal when used alone.

The co-operative effect of administration of individually suboptimal amounts of cpn10 and IFN-β is demonstrated in Example 6 of the specification. Example 6 data are presented in Figs. 8 and 9 and summarized in Table 4. The data in Table 4 clearly show that administration of cpn10 and IFN-β together gives a greater suppression of disability in the animal model than either agent administered alone. Therefore, Table 4 provides a clear pattern of the benefit of using the combined treatment as compared to using suboptimal amounts of the cpn10 or IFN-β alone.

The invention of claim 25 is directed to a method of treating MS through administering a combination of cpn10 and IFN-β in pharmaceutically effective amounts, where the resulting delay in MS relapse is greater than that of administering an equivalent amount of cpn10 or IFN-β alone. In the rejection of claim 1, the Examiner states with regard to the combination therapy that "Figure

[1] See, for example, specification, pages 12-13.

9 shows a very modest difference" and that there "is no evidence of a synergistic effect." Office Action, page 2.

The data presented in Fig. 9 and Table 4 clearly demonstrate a very distinct delay in disease relapse with the administration of the cpn10 and IFN-β combination as compared to the administration of either drug alone. The data supports claim 25 which states that the delay in MS relapse from the combination therapy is greater than that of administering an equivalent amount of cpn10 or IFN-β alone. Claim 25 does not specifically recite that the combination therapy result in a synergistic effect.

Neither Morton nor the MS Study, nor the combination thereof, teaches or suggests that cpn10 and IFN-β act in a co-operative manner or that a combination of cpn10 and IFN-β will provide a greater delay in MS relapse than the individual drugs administered alone in equivalent amounts.

The claimed invention is based on the discovery that cpn10 and IFN-β act via different mechanisms to co-operatively reduce EAE symptoms and decrease relapse frequency. At the priority date of the instant application, a skilled artisan would not have been able to predict an improved therapeutic effect from the combination of cpn10 and IFN-β administered in amounts which are suboptimal when administered alone. Nor would a skilled artisan have been able to predict a delay in MS relapse from the combination of cpn10 and IFN-β. Thus, Applicants respectfully submit that the cited references do not teach or suggest the claimed invention.

Even if it is suggested that a motivation to combine the references exists, which Applicants decidedly do not, the combination of references provide an 'obvious to try' situation at most. The court has "consistently held that 'obvious-to-try' is not to be equated with obviousness under 35 U.S.C. 103." *Gillette Co. v. S.C. Johnson & Son, Inc.*, 919 F.2d 720, 16 USPQ2d 1923 (Fed. Cir. 1990). An 'obvious-to-try' situation exists where a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosures, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that

the claimed result would be obtained if certain directions were pursued." *In re Eli Lilly & Co.*, 902 F.2d 943, 14 USPQ2d 1741 (Fed. Cir. 1990). Applicants respectfully submit that the references' teaching that cpn10 and IFN-β are individually effective in treating MS is not sufficient teaching that the combination of agents as claimed would provide a therapeutic effect.

In sum, Applicants respectfully submit that a *prima facie* case of obvious has not been made.

Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. §103.

CONCLUSION

Applicants believe that all issues raised in the Office Action have been properly addressed in this response. Accordingly, reconsideration and allowance of the pending claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, the Examiner is encouraged to contact Applicants' representative at the telephone number below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 524372000100. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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